DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

SEP 16

Kjng and Spalding
Attention: Jess Stribling
1730 Pennsylvania Avenue, N. W.
Washington, D.C. 20006-4706

Docket No. 98P-1291/CP1

Dear Mr. Stribling:

This is in response to your petition filed on December 21, 1998, and your amendments dated January 22, 1999, January 25, 1999 and July 27, 1999, requesting permission to file an Abbreviated New Drug Application (ANDA) for the following drug products: Oxycodone Hydrochloride/Oxycodone Terephthalate/Acetaminophen Tablets, 4.5 mg/0.38 mg/325mg and Oxycodone Hydrochloride/Oxycodone Terephthalate/Acetaminophen Tablets, 2.25 mg/0.19 mg/325 mg. The listed drug products to which you refer in your petition are Percodan® (Oxycodone Hydrochloride/Oxycodone Terephthalate/Aspirin) Tablets, 4.5mg/0.38mg/325 mg, and Percodan ® Demi (Oxycodone Hydrochloride/Oxycodone Terephthalate/Acetaminophen) Tablets, 2.25 mg/0.19mg/325 mg manufactured by Endo Pharmaceuticals.

We have reviewed your petition under Section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act (Act) and have determined that it is approved. This letter represents the Agency's determination that an ANDA may be submitted for the above-referenced drug products.

Your request involves a change in one active ingredient for another active ingredient of the same pharmacologic class in a fixed combination listed drug product [i.e., substituting an equipotent dose of acetaminophen (APAP) for aspirin (ASA) in the listed drug products]. The change you request is the type of change that is authorized under the Act.

Under Section 505(j)(2)(C)(i) of the Act, the Agency must approve a petition seeking a change in one active ingredient for another active ingredient of the same pharmacologic class in a fixed combination listed drug product unless it finds that investigations must be conducted to show the safety and effectiveness of the differing active ingredient (See 21 C.F.R. §314.93(c)(1)).

According to the Tentative Final Monograph (TFM) for OTC Internal Analgesic, Antipyretic, and Antirheumatic Products published November 16, 1988 in the Federal Register (53 FR 46204) the Agency believes at this time that it is reasonable for APAP and ASA to have the same dosage and frequency of administration because, based upon the data submitted to the Panel, the safe and effective dosage ranges for APAP and ASA are the same-325 mg to 650 mg every 4 hours, not to exceed 4 g in 24 hours (TFM, 53 FR at 46235). Accordingly, the Agency finds that the change in active ingredient for the specific proposed drug products does not pose

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questions of safety or effectiveness

In addition, this petition was evaluated with respect to the Regulations Requiring Manufacturers to Assess the Safety and Effectiveness of New Drugs and Biological Products in Pediatric Patients; Final Rule, published in the Federal Register (Pediatric Rule)(63 FR 66632). The agency has determined that your proposed change in active ingredient is subject to the Pediatric Rule and has concluded that investigations are not necessary to demonstrate the safety and effectiveness of your proposed products in the pediatric population, because the products do not represent a meaningful therapeutic benefit over existing therapies for pediatric patients and are not likely to be used in a substantial number of pediatric patients.

The Agency concludes, therefore, that investigations are not necessary in this instance. The pediatric study requirement is waived at this time but may be reevaluated if new information is available at the time you file your application. In addition, if shown to meet bioavailability requirements, the proposed drug products can be expected to have the same therapeutic effect as the listed reference drug products.

The approval of this petition to allow an ANDA to be submitted for the above-referenced drug products does not mean that the Agency has determined that an ANDA will be approved for the drug products. The determination of whether an ANDA will be approved is not made until the ANDA itself is submitted and reviewed by the Agency.

To permit review of your ANDA submission, you must submit all information required under Sections 505(j)(2)(A) and (B) of the Act. To be approved, the drug products will, among other things, be required to meet current bioavailability requirements under Section 505(j)(2)(A)(iv) of the Act. We suggest that you contact the Director, Division of Bioequivalence, at (301) 827-5847 to determine the specific requirements for these drug products. During the review of your application, the Agency may require the submission of additional information.

The listed drug products to which you refer in your ANDA must be the drug products upon which you based this petition. In addition, you should refer in your ANDA to the appropriate petition docket number cited above, and include a copy of this letter in the ANDA submission.

A copy of this letter approving your petition will be placed on public display in the Dockets Management Branch, Room 1061, Mail Stop HFA-305, 5630 Fishers Lane, Rockville, MD 20852.

Sincerely yours,'

Douglas L. Spom
Director
Office of Generic Drugs
Center for Drug Evaluation and Research